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Non-medical use of prescription opioids is associated with heroin initiation among US veterans

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Letters to the Editor

The journal publishes both invited and unsolicited letters.

NON-MEDICAL USE OF PRESCRIPTION OPIOIDS IS ASSOCIATED WITH HEROIN INITIATION AMONG US VETERANS

We read with interest the article by Banerjee and colleagues [1], entitled 'Non-medical use of prescription opioids is associated with heroin initiation among US veterans: a prospective cohort study', published in *Addiction*. The authors aimed to estimate the influence of non-medical use of prescription opioids (NMUPO) on heroin initiation among US veterans. They analyzed data from a prospective, multi-site, observational study of HIV-infected and an age/race/site-matched control group of HIV-uninfected veterans. A total of 3396 HIV-infected and uninfected patients were enrolled into the study. They found that non-medical use of prescription opioids (NMUPO) was associated positively and independently with heroin initiation. Banerjee *et al*. conclude that new-onset NMUPO is a strong risk factor for heroin initiation among HIV-infected and uninfected veterans in the United States [1].

We would like to comment that the major weakness of the study may be the sample bias, as the study used the subpopulation of VA patients who received care for infectious diseases such as HIV, hepatitis C virus (HCV) and others.

In 2014, a total of 10.3 million people reported using prescription opioids non-medically [2]. There was a significant decrease in the total number of non-medical use of prescription opioids (NMUPO) compared to 2010 (estimated 12.2 million) [3]. Paradoxically, the drop of 1.9 million NMUPO has not resulted in any improvement, neither in opioid mortality nor prevalence of heroin abuse or heroin mortality [4]. Ironically, there has been a significant increase in opioid overdose-related mortality, i.e. 16 007 deaths in 2012 but 18 893 deaths in 2014; namely, an 18% increase [5]. The number of people who used heroin peaked to 914 000 in 2014 versus 373 000 in 2007, a 145% increase [4]. Further, mortality related to heroin overdose has more than quintupled, from 1842 in 2000 to 10 574 deaths in 2014 [2], which is 2317 more than cited in Banerjee *et al*.'s [1] report.

In a recent review paper [6] entitled 'Relationship between nonmedical prescription-opioid use and heroin use', published in the *New England Journal of Medicine*, Compton *et al*. [6] opined that only a small percentage of non-medical users of prescription opioids initiate heroin use: '… the available data suggest that NMUPO is neither necessary nor sufficient for the initiation of heroin use…'. Indeed, Muhuri *et al*. found that 3.6% of non-medical users initiated heroin use within 5 years after beginning non-medical use of prescription opioids [7].

As acknowledged by Banerjee *et al*., 'the study enrolled individuals who are probably at higher risk for heroin initiation than the general veteran population', therefore their results should not be generalized to other VA patients, as the title of the paper reflects. Indeed, a study of new HCV infections in Massachusetts found that 95% of interview respondents used prescription opioids before initiating heroin [8]. One study suggests that using opioid pain relievers before transitioning to heroin injection is a common trajectory for young injection drug users with HCV infection [9]. This may be the underlying reason that the rate of heroin initiation in non-HIV-exposed is significantly higher than the rate observed among US adults.

Declaration of interests

XR has received speaker's fees in the past three years from Cephalon, Purdue, Insys, Zogenix, DepoMed, Iroko, Horizon, and Mallinckrodt. AK has received speaker's fees in the past three years from Merck and Gralise.

Keywords Hepatitis C, heroin, HIV, NMUPO, prescription opioids, veterans.

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References

1. Banerjee G., Edelman E. J., Barry D. T., Becker W. C., Cerdá M., Crystal S. *et al.* Non-medical use of prescription opioids is associated with heroin initiation among US veterans: a prospective cohort study. *Addiction* 2016; **111**: 2021–31.
2. Center for Behavioral Health Statistics and Quality *2014 National Survey on Drug Use and Health: Detailed Tables*. Rockville, MD: Substance Abuse and Mental Health Service Administration; 2015.

3. Meyer R., Patel A. M., Rattana S. K., Quock T. P., Mody S. H. Prescription opioid abuse: a literature review of the clinical and economic burden in the United States. *Popul Health Manag* 2014; **17**: 372–87.
4. Ruan X., Wyche M. Q. III, Kaye A. D. Analyzing the relationship between nonmedical prescription-opioid use and heroin use. *J Opioid Manag* 2016; **12**: 11–14.
5. Centers for Disease Control and Prevention. National Vital Statistics System, Mortality file. Number and age-adjusted rates of drug-poisoning deaths involving opioid analgesics and heroin: United States, 1999–2014. Available at: http://www.cdc.gov/nchs/data/health_policy/AADR_drug_poisoning_involving_OA_Heroin_US_2000-2014.pdf (accessed 27 October 2016) (Archieved at http://www.webcitation.org/6lZ0N8gPN).
6. Compton W. M., Jones C. M., Baldwin G. T. Relationship between nonmedical prescription-opioid use and heroin use. *N Engl J Med* 2016; **374**: 154–63.
7. Muhuri P. K., Gfroerer J. C., Davies M. C. Subtance Abuse and Mental Health Services Administration (SAMHSA). Associations of nonmedical pain reliever use and initiation of heroin use in the United States. Available at: http://www.samhsa.gov/data/sites/default/files/DR006/DR006/nonmedical-pain-reliever-use-2013.htm (accessed 13 November 2016) (Archived at http://www.webcitation.org/6m0MYw9lf).
8. Centers for disease Control and Prevention. Notes from the field: risk factors for hepatitis C virus infections among young adults—Massachusetts, 2010. *Morb Mortal Wkly Rep* 2011; **60**: 1457.
9. Klevens R. M., Hu D. J., Jiles R., Holmberg S. D. Evolving epidemiology of hepatitis C virus in the United States. *Clin Infect Dis* 2012; **55**: S3–9.

REPLY TO RUAN *ET AL.* (2017): NON-MEDICAL USE OF PRESCRIPTION OPIOIDS IS ASSOCIATED WITH HEROIN INITIATION AMONG US VETERANS

We thank Ruan and colleagues for their letter and appreciate their comments regarding our recent study [1], which demonstrated an independent association between non-medical use of prescription opioids (NMUPO) and heroin initiation among US veterans [2]. Our results indicate that participants who reported prior or concurrent NMUPO had 5.43 times the adjusted hazard of heroin initiation, compared to participants who reported no NMUPO [95% confidence interval (CI) = 4.01–7.35]. While we acknowledge in our paper that these results are not necessarily generalizable to all US veterans, given the inclusion of participants who are HIV-infected and/or hepatitis C virus (HCV)-infected, the observed effect of NMUPO on risk for heroin initiation was robust to sensitivity analyses. For example, as described in our published study, excluding the 701 HCV-positive participants did not affect the result [adjusted hazard ratio (AHR) = 6.21, 95% confidence interval (CI) = 4.54–8.51)] meaningfully. In light of the concerns raised by Ruan and colleagues, we repeated the analysis excluding HIV-infected individuals, and in fact found that the relationship between NMUPO and heroin initiation was stronger (AHR = 7.01, 95% CI = 5.40–9.09). Thus, although the observed absolute rate of heroin initiation may be greater than in the general US veteran population due to the specific inclusion of higher-risk patients, it does not appear that the relationship between NMUPO and heroin initiation is affected by HCV or HIV prevalence.

Ruan and colleagues also highlighted the increase in heroin-related deaths from 2013 to 2014, with the concurrent decrease in people reporting non-medical use of prescription opioids. This inverse relationship may, in fact, be attributable to the fact that large numbers of people who developed opioid use disorder (as a result of non-medical use of prescription opioids) have transitioned subsequently to heroin use [3,4]. The trend between increased rates of death associated with heroin use and decreased rates of death associated with use of prescription opioids thus speaks to the potential role of transitioning from the misuse of prescription opioids to the use of heroin in many parts of the country [5,6]. This phenomenon is consistent with the findings of our paper, given that NMUPO may be one step in a complex, multi-step cascade that increases risk of transition to heroin use in the population [7,8].

Additionally, while Compton and colleagues noted that: 'only a small percentage of non-medical users of prescription opioids initiate heroin use', they also go on to say that: 'given the large number of nonmedical users, even a small percentage who initiate heroin use translates into several hundred thousand new heroin users' [9]. Ruan *et al.* cite a statistic that 3.6% of the people reporting NMUPO initiated heroin use within 5 years of beginning NMUPO. Indeed, even this small percentage, if correct, would result in approximately 370 800 individuals initiating heroin use by 2019. Prior and subsequent years would contribute similar proportions of individuals initiating heroin due to NMUPO [10].

In conclusion, we appreciate that the rates of heroin initiation in our study are potentially higher compared to rates of heroin initiation among studies that do not include HIV- and HCV-infected veterans. However, this limitation does not obscure the primary findings of our study, which speaks to the observed increased relative risk of heroin initiation among participants who report prior/concurrent NMUPO compared to participants who report no prior/concurrent NMUPO.

Declaration of interests

None.